PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 43842	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/IL2008/001105	International filing date *(day/month/year)* 11.08.2008	Priority date *(day/month/year)* 13.08.2007
International Patent Classification (IPC) or national classification and IPC INV. A61B5/053		
Applicant Cheetah Medical Ltd.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
2009-06-29	04.11.2009

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IL2008/001105

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-36 as originally filed

   Claims, Numbers

   9, 11, 13, 15-20, 22-39, 42-46 filed with telefax on 29.06.2009

   Drawings, Sheets

   1/63-63/63 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☒ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☒ the claims, Nos. 1-8,10,12,14,21,40,41
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

5. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 70.2 (e)).

6. ☐ Supplementary international search report(s) from Authority(ies) have been received and taken into account in drawing up this report (Rule 45bis.8(b) and (c)).

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	9,11,13,15-20,22-39,42-46
	No:	Claims	
Inventive step (IS)	Yes:	Claims	9,11,13,15-20,22-39,42-46
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	9,11,13,15-20,22-39,42-46
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: US 2005/004609 A1 (STAHMANN JEFFREY E [US] ET AL) 6 January 2005 (2005-01-06)
   D7: US 2004/133123 A1 (LEONHARDT STEFFEN [DE] ET AL) 8 July 2004 (2004-07-08)
   D9: WO 2006/087696 A (NEW LEAF CAPITAL LTD [GB]; KEREN HANAN [IL]; SIMON AVRAM B [GB]) 24 August 2006 (2006-08-24) cited in the application

2.1 The document D1 is regarded as being the closest prior art to the subject-matter of claim 9, and shows (the references in parentheses applying to this document):

A method of analyzing an input radiofrequency signal sensed from an organ of a subject, comprising:

- processing said input radiofrequency signal to provide a processed input signal (paragraphs 19, 22, 24);
- filtering said signal using a dynamically variable band pass filter adapted in response to a change in a physiological condition of the subject, thereby providing a filtered signal (paragraph 25).
- the filtered signal is used for determining blood flow (end of paragraph 25)

2.2 The subject-matter of claim 9 differs from this known method in that
   1) the processing comprises determining a phase shift of said input signal relative to an output radiofrequency signal transmitted to the organ; and
   2) the filtering is done on the processed rather than the raw input signal.

2.3 The subject-matter of claim 9 is therefore new (Article 33(2) PCT).

2.4 The problem to be solved by the present invention may be regarded as providing an alternative method of analyzing impedance signals.

2.5 The solution to this problem proposed in claim 9 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

While document D9 discloses feature 1 (see page 21, lines 3-9 and page 28, line 7 - page 29, line 5 and Fig. 2), it does not disclose feature 2, i.e. to first determine a phase shift and then filter the signal. While the order of the filtering and processing steps is not always quite clear from D9, the flowchart shown in Fig. 8 suggests that the signal is first filtered and then processed by determining the phase shift. Furthermore, the adaptive filters disclosed in document D7 are used to separate different kinds of signals (respiratory and cardiac) rather than for noise reduction. Document D1 discloses some basic signal processing before the signal is passed on to the adaptive filter (see Fig. 2), but does not hint at determining a phase shift. Also, the adaptive filter, which appears to be a high pass filter rather than a band pass filter (see D1, paragraphs 30-31; D1 also discloses a band pass filter, which is however not adaptive and acts on the raw signal, see paragraph 28), is used to separate different kinds of signals rather than for noise reduction (cf. D7). Given the different orders of processing and filtering disclosed in D1 and D9, it would not be obvious for a person skilled in the art to combine these two documents. The subject-matter of claim 9 therefore involves an inventive step.

2.6 This reasoning also applies, *mutatis mutandis*, to the subject matter of claim 20, which therefore is also considered new (Article 33(2) PCT) and inventive (Article 33(3) PCT).

2.7 Claims 11, 13, 15-19, 22-39 and 42-46 are dependent on claim 9 or claim 20, respectively and as such also meet the requirements of the PCT with respect to novelty and inventive step.

WHAT IS CLAIMED IS:

1-8 (Canceled)

9. A method of analyzing an input radiofrequency signal sensed from an organ of a subject, comprising:

processing said input radiofrequency signal to provide a processed input signal, wherein said processing comprises determining a phase shift of said input signal relative to an output radiofrequency signal transmitted to the organ;

filtering said processed signal using a dynamically variable band pass filter adapted in response to a change in a physiological condition of the subject, thereby providing a filtered signal; and

using said filtered signal and said phase shift for calculating at least one of: a stroke volume, a cardiac output, a brain intra luminal blood volume and blood flow.

10. (Canceled)

11. The method of claim 9, wherein said possessing comprises filtering said input radiofrequency signal using an analog filter.

12. (Canceled)

13. The method of claim 9, wherein said blood flow comprises at least one of: an external carotid blood flow rate, an internal carotid blood flow rate, an ulnar blood flow rate, a radial blood flow rate, a brachial blood flow rate, a common iliac blood flow rate, an external iliac blood flow rate, a posterior tibial blood flow rate, an anterior tibial blood flow rate, a peroneal blood flow rate, a lateral plantar blood flow rate, a medial plantar blood flow rate and a deep plantar blood flow rate.

14. (Canceled)

15. The method of claim 9, further comprising transmitting said output radiofrequency signal to the organ and sensing said input radiofrequency signal from the organ.

16. The method of claim 9, further comprising reducing or eliminating amplitude modulation of said input radiofrequency signal, so as to provide a signal of substantially constant envelope.

17. The method of claim 16, wherein said reducing or eliminating said amplitude modulation comprises maintaining a phase modulation of said input radiofrequency signal.

18. The method of claim 9, further comprising mixing said input radiofrequency signal and an output radiofrequency signal transmitted to the organ so as to provide a mixed radiofrequency signal.

19. The method of claim 18, wherein said mixing comprises providing a radiofrequency sum and a radiofrequency difference.

20. Apparatus for analyzing an input radiofrequency signal sensed from an organ of a subject, comprising:

an input unit for receiving the input radiofrequency signal;

a signal processing unit for processing said input radiofrequency signal to provide a processed input signal, said processing unit comprising a phase shift determinator configured for determining a phase shift of said input signal relative to an output radiofrequency signal transmitted to the organ;

a filtering unit configured for filtering said processed signal using a dynamically variable band pass filter adapted in response to a change in a physiological condition of the subject, to thereby provide a filtered signal; and

a data processor for calculating at least one quantity based on said phase shift, wherein said at least one quantity is selected from the group consisting of a stroke volume, a cardiac output, a brain intra luminal blood volume and blood flow.

21. (Canceled)

22. The method or apparatus of any of claims9, 11, 13 and 15-20, wherein said physiological condition is a heart rate of the subject.

23. The method or apparatus of claim 22, wherein at least one of a lower frequency bound and an upper frequency bound characterizing said filter is a linear function of said heart rate.

24. The method or apparatus of claim 23, wherein said lower frequency bound is about 0.9*(HR/60) Hz at all times, wherein said HR is said heart rate in units of beats per minute.

25. The method, device, system or apparatus of claim 23, wherein said upper frequency bound is about 6 + 1.5*[(HR/60) - 1] Hz at all times, wherein said HR is said heart rate in units of beats per minute.

26. The method or apparatus of claim 22, wherein said heart rate is determined from an ECG signal received from said subject.

27. The method or apparatus of any of claims9, 11, 13, 15-20, 22-26, wherein an upper frequency bound characterizing said filter is determined using an iterative process.

28. The method or apparatus of claim 27, wherein said iterative process is based on a comparison between a value of a physiological parameter as extracted from said filtered input signal and a value of said physiological parameter as extracted from a reference signal.

29. The method or apparatus of claim 28, wherein said reference signal comprises an ECG signal

30. The method or apparatus of claim 27, wherein each iteration of said iterative process comprises:

if said comparison meets a predetermined criterion , then updating said upper frequency bound by calculating an average between a low threshold and a high threshold;

said thresholds being predetermined or set in a previous iteration of said iterative process.

31. The method or apparatus of claim 28, wherein said physiological parameter is a ventricular ejection time (VET).

32. The method or apparatus of claim31, wherein said VET is averaged over a plurality of heart beats.

33. The method or apparatus of claim 31, wherein said VET is extracted from an average heart beat morphology of the subject.

34. The method or apparatus of claim 27, wherein said physiological condition is a heart rate of the subject.

35. The method or apparatus of claim 34, wherein an initial value of said upper frequency bound in said iterative process is a linear function of said heart rate.

36. The method or apparatus of claim 35, wherein an initial value of said upper frequency bound in said iterative process is about 6 + 1.5*[(HR/60) - 1] Hz, wherein said HR is said heart rate in units of beats per minute.

37. The method or apparatus of claim 9 or 20, wherein said input radiofrequency signal is indicative of impedance the organ.

38. The method or apparatus of claim 9 or 20, wherein said input radiofrequency signal is indicative of hemodynamic reactance of the organ.

39. The apparatus of claim 20, wherein said signal possessing unit comprises an analog filter for filtering said input radiofrequency signal.

40. (Canceled)

41. (Canceled)

42. The apparatus of claim 20, wherein said signal processing unit comprises an envelope elimination unit designed and configured to reduce or eliminate amplitude modulation of said filtered signal, so as to provide a signal of substantially constant envelope.

43. The apparatus of claim 42, wherein said envelope elimination unit is designed and configured to maintain a phase modulation of said signal.

44. The apparatus of claim 20, wherein said signal processing unit comprises a mixer designed and configured to mix said input radiofrequency signal and said output radiofrequency signal transmitted to the organ so as to provide a mixed radiofrequency signal.

45. The apparatus of claim 44, wherein said mixer is operable to provide a radiofrequency sum and a radiofrequency difference.

46. A system for monitoring at least one electrical property of an organ of a subject, comprising:

a radiofrequency generator for generating an output radiofrequency signal;

a plurality of electrodes, designed to be connectable to the skin of the subject, said electrodes being for transmitting said output radiofrequency signal to the organ and for sensing an input radiofrequency signal from the organ; and

the apparatus according to any of claims 20, 22-39 and 42-45.